II. Remarks

No new matter is added by the amendments.

Support for the amended description of the polymeric delivery system in Amended Claim 1 – "polymers capable of entrapping and controlling the release of the at least one active ingredient" – is found at least in Paragraphs [0018] and [0050].

Support for the amended viscosity ranges of the first and second emulsion formulations in Amended Claim 1 – less than about 25,000 cps – is found in at least Paragraph [0069].

Support for the amended description of the first and second formulations in Amended Claim 1 as emulsions is found at least in Paragraph [0069].

Support for the more detailed recitation of the polymeric delivery system as being cross-linked and non-swellable in Amended Claim 2 and the specific polymeric delivery systems recited in the Markush group in Amended Claim 3 are found at least in Paragraphs [0050] to [0054].

Support for the amendment to Claim 5 is found at least in Paragraph [0029].

Support for the addition of retinol to Amended Claim 10 is found at least in original claims 17, 21 and 22 and Paragraph [0047].

A. Required Claim Elements are Well-Defined in Specification

In the third line of the first full paragraph of Page 7, the Office Action states that the term "substantially the same lipophilicity" is not defined in the Specification. Applicants respectfully traverse. As explained at the Interview, in Paragraph [0068] Applicants define the phrase "substantially the same lipophilicity" in terms of the partition coefficient of each carrier base. To paraphrase this paragraph, "the requirement [that the two emulsions have substantially the same lipophilicity] is met if the partition coefficients [of

the two emulsions] vary by no more than 10%, advantageously by no more than 5%, preferably by no more than 2.5%."

In the last line on Page 8 carrying over to the first line of Page 9, the Office Action states that the term "polymeric delivery system" is not defined in the Specification. As explained at the Interview, Paragraph [0018] of the Specification defines a polymeric delivery system in terms of polymer particles that control the rate of release of the entrapped active ingredient. Paragraph [0050] of the Specification further defines polymeric delivery system as "particles (*e.g.*, microparticles), aggregates of particles (e.g. aggregates of microparticles) or clusters of aggregates (agglomerates) of particles (e.g. agglomerates of microparticles) which are capable of entrapping any desired active for delayed release." This paragraph continues to describe the polymeric delivery system as typically being cross-linked. This limitation is recited in Amended Claim 2. Specific examples of polymeric delivery systems are recited in Amended Claim 3.

B. The Office Action Fails to Make a *Prima Facie* Case of Obviousness

Each of the pending claims requires first and second emulsion formulations comprised of "water-based carrier bases having substantially the same lipophilicity." This is a key element of the present invention. As explained in the Interview with the Examiner and again below, failure to match the lipophilicities of the emulsions (*i.e.*, have "substantially the same lipophilicity") will result in either dose dumping or ineffectual delivery of an active ingredient entrapped within a polymeric delivery system. Applicants therefore respectfully submit that the cited prior art references, when viewed in combination, fail to teach or suggest this limitation.

WO 93/15726 ("WO26") – the primary reference that forms the basis for all of the pending rejections – does not teach or suggest creating a combination formulation from two component formulations each having substantially the same lipophilicity. To the contrary, WO26 teaches two component formulations – (i) an aqueous solution of clindamycin and (ii) an aqueous suspension of benzoyl peroxide ("BPO") – which, when combined, form a final, thickened aqueous gel having a viscosity far in excess of what is claimed by Applicants. In short, the formulations taught in WO26 do not have lipophilic

components and are not emulsions as recited in the amended claims. *See* Nacht Declaration at ¶ 8.

Moreover, WO26 teaches admixing a BPO suspension having a viscosity of from 50,000 to 90,000 cps with a clindamycin suspension, resulting in a final formulation having viscosity of from 70,000 to 120,000 cps. *See* WO26 at page 8. As explained by the Applicants at the Interview, in order for the dispense means of the present invention to work in the claimed manner (*i.e.*, to permit dispense of the first formulation in a specific ratio to the second formulation), the viscosities of the two formulations must not only be matched to within a certain percentage of each other (*see* Previously Amended Claims 33 – 35), the formulations must have viscosities of less than about 25,000 cps (Amended Claim 1), preferably less than about 20,000 cps (*see* Previously Amended Claim 34), and still more preferably less than about 10,000 cps (*see* Previously Amended Claim 35). *See* Nacht Declaration at ¶¶ 9 – 10.

Applicants respectfully submit that the Office Action does not provide a clearly-articulated rationale explaining why a person having ordinary skill would have been motivated to modify the benzoyl peroxide / clindamycin aqueous gel taught in WO26 in a manner to create an emulsion having viscosities recited in Currently Amended Claim 1, and Previously Amended Claims 31 and 32.

In addition, as explained by the Applicants at the Interview, the carboxy vinyl polymer taught in WO26 is a swellable polymer – specifically a gelling agent – and is not a polymeric delivery system of the type recited in the amended claims (*i.e.*, polymers capable of entrapping and controlling the release of at least one active ingredient). *See* Nacht Declaration at ¶ 11. On this point, Applicants incorporate by reference the remarks made in the Expert Declarations of Drs. Katz and Lochhead. *See* Katz Declaration at ¶¶ 12 – 13; *see also* Lochhead Declaration at ¶ 11. Applicants thus respectfully submit that the Office Action does not provide a clearly-articulated rationale explaining why a person having ordinary skill would have been motivated to modify the benzoyl peroxide / clindamycin combination taught in WO26 by substituting a polymeric delivery system of the type claimed by the Applicants with a carboxyvinyl polymer as taught in WO26.

At page Page 5, the Office Action suggests adding the polymeric delivery system taught in European Patent Application EP 306236 to the formulations taught in WO26. At the Interview, Applicants explained that because the carrier systems taught in WO26 do not have lipophilic components adding a polymeric delivery system of the type taught in EP 306236 would result in an ineffective final formulation.

Clindamycin is a water-soluble, hydrophilic ingredient. Impregnating such an ingredient into a porous solid particle polymeric delivery system – one in which the pores form a continuous network open to the exterior of the particles, permitting the outward diffusion of the impregnant at a controlled rate – and adding the resulting "loaded" delivery system into the aqueous formulations taught in WO26 would result in "dose dumping." The rate of delivery of the clindamycin would not be controlled in such a formulation, thereby defeating the purpose of having a controlled-release delivery system. *See* Nacht Declaration at ¶ 12.

In contrast, benzoyl peroxide is a lipophilic active ingredient. Since the formulations taught in WO26 do not have lipophilic components, a delivery system according to EP 306236 loaded with BPO would not deliver the active ingredient (*i.e.*, the BPO) in the formulations taught in WO26. *See* Nacht Declaration at ¶ 13.

III. Conclusion

In summary, an obviousness determination requires "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *See, In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995) (emphasis added). *Accord*, *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974))("obviousness requires a suggestion of all limitations in a claim.") Applicants respectfully submit that several of the critical limitations recited in the amended claims – two emulsions, each having substantially the same lipophilicity, each having viscosities of less than about 25,000, where the viscosities are matched so as not to vary by no more than 10%, 5% or 2.5% -- are neither taught nor suggested by the cited references in a manner that would give a person having ordinary skill in the art a reasonable expectation of achieving the claimed invention without undue experimentation.

For the above reasons, it is respectfully submitted that the claims as presented are in condition for allowance. Favorable action is therefore earnestly solicited. Should the Examiner believe that a further interview would expedite allowance, please contact undersigned counsel.

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Respectfully submitted,

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